

DETAILED ACTION

Applicants' response, which included cancellation of withdrawn claims 2-5, filed on 02/21/2012, is made of record. Claims 1 and 6-14 are pending. In view of applicants' response, the following rejections made in the previous office action are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 and 6-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hill et al. WO 01/85702 (equivalent US 2004/0006097) in view of Beck et al., Rosen et al., (all cited in the IDS) and Wade et al.

1. Determining the scope and contents of the prior art:

The claimed invention relates to a process of preparation of compound (7) by converting the halo compound (1) to the alcohol (2), oxidation of alcohol (2) to aldehyde

(3), condensation of aldehyde (3) with pyrimidine compound (4) to get compound (5) followed by an oxidation of compound (5) to obtain compound (6) and compound (7).

The overall process steps are known in the art.

Hill teaches process of making rosuvastatin which includes the same process of Wittig-Horner condensation of an aldehyde with pyrimidine compound. See pages 1-13 for the details of the process. Especially see Scheme 2, compound D and compound E. Note compound E is analogous to compound (3) of instant claims.

Thus, Hill clearly teaches the overall process of making of rosuvastatin using Wittig-Horner reaction

2. Ascertaining the differences between the prior art and the claims at issue:

The claimed invention requires use of aldehyde of formula (3) while Hill teaches analogous aldehyde of formula E.

Beck teaches a process of preparing various statin analogs using Wittig-Horner condensation which includes aldehyde of formula (3). See entire documents for the process of making and various compounds made. Especially see page 54, Scheme 1 for the overall process and for compound 5 and compound 6. Beck differs in not teaching synthesis of rosuvastatin. However, Beck teaches the generality of the overall process and hence one trained in the art would be motivated to combine the teaching of Hill and Beck and make rosuvastatin.

Instant claim 1 requires process for making the compound (3) from halo compound (1). Beck states compound 5 is made from glucose, but provides no details (page 54, last paragraph).

Rosen teaches process of making such compounds and their use in Wittig-Horner reaction. See entire document. Especially see Scheme III and Scheme V. See compound 19, 31, 36 and 37. Rosen clearly teaches how to make compound of formula (3) from compound (2).

Rosen, though teaches halo compound 36, does not teach the conversion of instant halo compound (1) to make the corresponding alcohol.

But such conversion of halides to alcohols is well known in the art, even text book of organic chemistry.

For example Wade teaches such a conversion. See entire document. Especially see Scheme 1, conversion of compound 2 to compound 4 and Scheme 2, conversion of compound 6 to compound 7.

3. Resolving the level of ordinary skill in the pertinent art:

Thus, one having ordinary skill in the art at the time of the invention was made would have been motivated to combine the teachings of Hill, Beck, Rosen and Wade and employ the process rosuvastain and its analogs as taught by these prior art, including the process of making aldehyde of formula (3) and expect to obtain the desired product because he would have expected the analogous materials behave similarly in view of the combine teaching of the prior art. It has been held that application of an old process to an analogous material to obtain a result consistent with the teachings of the art would have been obvious to one having ordinary skill. Note In re Kerkhoven 205 USPQ 1069.

Also see *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007), wherein the court stated that

[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Such is the case with instant claims.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness:

Specification has no comparative example showing unexpected superior results.

This rejection is same as made in the previous office action. Applicants' traversal to overcome this rejection is not persuasive.

Contrary to applicants' assertion, compound of formula (3) and the compound (E) of prior art are structural analogs and one expect them to behave similarly in a Wittig reaction or Wittig-Horner reaction absence of any direct evidence. In instant compound (3), the carboxylate and one of the hydroxyl is protected as lactone while in the prior art compound, the carboxylate is protected as an ester and the hydroxyl is separately protected. They are therefore structural analogs and the reacting group is same in both cases. Applicants have argued that the pKa values of these are different. But such an argument is not a valid argument. First, criticality of pKa is not shown in the specification and the alleged pKa difference of 30 and 25 would alter the reactivity of compound (E)

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has no factual support. Secondly, applicants' argument pertaining to deprotonation and attack on aldehyde is unclear and confusing. Contrary to applicants' urging, compound (E) will not undergo deprotonation as there is no such free acidic hydrogen in compound (E) and the attack on aldehyde is essential for Wittig and Horner-Emmon reaction.

In fact, instant compound (3) can undergo deprotonation when P^1 is H and hinder the Horner-Emmon reaction. Also there is no showing of unexpected superior results when P^1 is H.

Applicants' argument that Beck should not be combined with Hill lacks factual support. Applicants have argued that Hill uses phosphorous oxide bearing reagent while Beck uses phosphonium salt for the Wittig and Horner-Emmon reaction Wittig reaction. But both these reagents work in the condensation reaction (Wittig and Wittig and Horner-Emmon reaction) and the overall reaction is same in both cases. Furthermore, applicants' choice of R^6 includes both these reagents and hence it is not clear how applicants can claim these reagents are not the same as in Hill and Beck. As for applicants' argument that Beck did not teach the process of making the alcohol, Beck clearly states the alcohol can be made by the known process and refers Yang. What is known need not be taught again. As for applicants argument that one trained in the art would not know how to convert an iodide of Rosen to alcohol, nucleophilic displacement of iodide by nucleophile is known in the art (see Yang & Wade) and one trained would be able to perform such an hydrolysis absence of unexpected superior results.

Hence, this rejection is proper and is maintained.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 6-14 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-5 of copending Application No. 11/721,858 in view of Beck cited above. The overall process of the claimed invention is also embraced in the claims 1-5 of the later filed copending application. Although specific pyrimidine compound of formula (7) is excluded by a proviso, the generality of the process is clearly taught in the claims 1-5 and prior art. Beck shows Wittig-Horner condensation can be used for making various statins with aldehyde of formula (3). Hence, instant process is an obvious variant.

This is a provisional obviousness-type double patenting rejection.

This rejection is same as made in the previous office action. Applicants have differed addressing this rejection. For reasons stated above, this rejection is proper and is maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624